We claim:

1. An isolated DNA molecule useful for the diagnosis or therapy of osteoporosis, selected from the group consisting of:

(a) a DNA molecule having a nucleotide sequence encoding an amino acid sequence as shown in Figure 2;

(b) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (a), and which encodes a protein that, when introduced into human osteoblasts, increases the ability of the osteoblasts to synthesize bone;

(c) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (b) and which encodes a protein that, when introduced into osteoblast cells of humans, increases the ability of the cells to synthesize bone;

(d) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (a), and which encodes a protein that, when introduced into endothelial cells of humans, increases the ability of the endothelial cells to form vascular tissue; and

(e) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (d), and which encodes a protein that, when introduced into cells of humans, increases the ability of the cells to form vascular tissue.

2. A nucleic acid used for a method of determining predisposition to osteoporosis of a human subject by incubating the nucleic acid with nucleic acid sequences derived from a sample from the subject, the nucleic acid consisting of at least 10 consecutive nucleotides of a DNA sequence selected from the sequence shown in Figure 2 or a complementary strand of said sequence.

3. A nucleic acid as described in claim 2, wherein the method of incubating the nucleic acid with nucleic acid sequences derived from a sample of the subject utilizes incubation conditions of 750 mM NaCl, 50 mM NaPhosphate, 5 mM EDTA, pH 7.4 and a temperature of 25-30 degrees C.

4. A nucleic acid used for a method of determining predisposition to osteoporosis of a human subject according to claim 3 wherein the nucleic acid consists of at least 25 consecutive nucleotides of a DNA sequence.

5. An expression vector comprising a promoter that is operably linked with a DNA molecule useful for the diagnosis or therapy of osteoporosis, the DNA molecule selected from the group consisting of:

(a) a DNA molecule having a nucleotide sequence encoding an amino acid sequence as shown in Figure 2;

(b) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (a), and which encodes a protein that, when introduced into human osteoblasts, increases the ability of the osteoblasts to synthesize bone;

(c) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (b) and which encodes a protein that, when introduced into osteoblast cells of humans, increases the ability of the cells to synthesize bone;

(d) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (a), and which encodes a protein that, when introduced into endothelial cells of humans, increases the ability of the endothelial cells to form vascular tissue; and

(e) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (d), and which DNA molecule encodes a protein that, when introduced into endothelial cells of humans, increases the ability of the endothelial cells to form vascular tissue, wherein the expression vector codes for a transmembrane protein that modulates bone density.

6. A method for modulating bone density, the method comprising the step of introducing an expression vector into a bone cell, wherein the expression vector comprises a promoter that is operably linked with a DNA molecule useful for the diagnosis or therapy of osteoporosis, the DNA molecule selected from the group consisting of:

(a) a DNA molecule having a nucleotide sequence encoding an amino acid sequence as shown in Figure 2;

(b) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (a), and which encodes a protein that, when introduced into human osteoblasts, increases the ability of the osteoblasts to synthesize bone;

(c) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (b) and which encodes a protein that, when introduced into osteoblast cells of humans, increases the ability of the cells to synthesize bone;

(d) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (a), and which encodes a protein that, when introduced into endothelial cells of humans, increases the ability of the endothelial cells to form vascular tissue; and

(e) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (d), and which DNA molecule encodes a protein that, when introduced into endothelial cells of humans, increases the ability of the endothelial cells to form vascular tissue.

7. A method of using an expression vector to select a test ligand that modulates bone density, comprising the steps of:

(a) introducing the expression vector into a host cell to produce a recombinant host cell that expresses the receptor on its surface;

(b) culturing the recombinant host cell; and

(c) assaying binding either directly or indirectly between the expressed receptor from the cultured recombinant host cell and the test ligand,

wherein the expression vector comprises a promoter that is operably linked with a DNA molecule useful for the diagnosis or therapy of osteoporosis, the DNA molecule selected from the group consisting of:

(i) a DNA molecule having a nucleotide sequence encoding an amino acid sequence as shown in Figure 2;

(ii) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (a), and which encodes a protein that, when introduced into human osteoblasts, increases the ability of the osteoblasts to synthesize bone;

(iii) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (ii) and which encodes

a protein that, when introduced into osteoblast cells of humans, increases the ability of the cells to synthesize bone;

(iv) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (i), and which encodes a protein that, when introduced into endothelial cells of humans, increases the ability of the endothelial cells to form vascular tissue; and

(v) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (iv), and which DNA molecule encodes a protein that, when introduced into endothelial cells of humans, increases the ability of the endothelial cells to form vascular tissue.

8. A method of regulating bone strength and mineralization by activating a bone density regulating transmembrane receptor encoded by an isolated DNA molecule useful for the diagnosis or therapy of osteoporosis, selected from the group consisting of:

(a) a DNA molecule having a nucleotide sequence encoding an amino acid sequence as shown in Figure 2;

(b) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (a), and which encodes a protein that, when introduced into human osteoblasts, increases the ability of the osteoblasts to synthesize bone;

(c) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (b) and which encodes a protein that, when introduced into osteoblast cells of humans, increases the ability of the cells to synthesize bone;

(d) a DNA molecule capable of specific hybridization under stringent conditions to a DNA molecule according to (a), and which encodes a protein that, when introduced into endothelial cells of humans, increases the ability of the endothelial cells to form vascular tissue; and

(e) a DNA molecule having a nucleotide sequence which is degenerate as a result of the genetic code to the encoded protein amino acid sequence according to (d), and which encodes a protein that, when introduced into endothelial cells of humans, increases the ability of the endothelial cells to form vascular tissue,

wherein the method comprises a first step of providing a ligand of the transmembrane receptor and a second step of administering the provided ligand in a medically acceptable form.

9. A method as described in claim 8, wherein the ligand is selected from the group consisting of: RVRLASHLRKLRKRLLR (SEQ ID NO:83); RLTRKRGLKLA (SEQ ID NO:76); CRAKRNNFKSA (SEQ ID NO:77); LKWKS (SEQ ID NO:78); KIRVKAGETQKKVIFCSREKVSHL (SEQ ID NO:79); FIPLKPTVKMLERSNHVSRTEVSSNHV (SEQ ID NO:80); DKGMAPALRHLYKELMGPWN (SEQ ID NO:81) and DALKLAIDNALSIT (SEQ ID NO:82)

10. A method for determining bone strength and mineralization predisposition of a patient, the method comprising the steps of:

(a) providing a patient sample that contains nucleic acid that encodes the BSMR protein and;

(b) analysing the sample from step (a) to determine whether the contacting the sample of (a) with one or more second nucleic acid(s) having at least one sequence described by claim 1 under conditions of hybridization; and

(c) detecting the formation of a hybrid between the sample nucleic acid and the second nucleic acid.

11. A method for determining bone strength and mineralization predisposition of a patient from analysis of epitopes on the bone strength and mineralization regulator protein, the method comprising the steps of:

(a) providing a tissue or blood sample of the patient;

(b) contacting the sample from step (a) with at least one conjugate of an antibody or antibody fragment with a reporter molecule, wherein the antibody or antibody fragment recognizes one or more epitopes of the bone strength and mineralization regulator protein; and

(c) detecting the formation of a complex between the conjugate and protein within the sample.

12. A method as described in claim 11, wherein step (b) utilizes at least two different conjugates that bind to at least two different portions of the bone strength and mineralization regulator protein.

13. A method as described in claim 12, wherein one of the conjugates binds to an epitope within the amino terminal half of the protein and a second of the conjugates binds to an epitope outside the amino terminal half of the protein.

14. A method for enhancing bone strength and mineralization by a mammalian cell, the method comprising the step of introducing the expression vector of claim 5 into the cell.

15. A method of increasing bone strength and mineralization in a human subject, comprising the steps:

(a) providing a ligand and/or a protease of the bone strength and mineralization regulator protein; and

(b) administering the ligand and/or protease to the human subject.

16. A method as described in claim 15, wherein step (b) is carried out by injection or by oral delivery.

17. A method as described in claim 15, wherein the ligand is selected from the group consisting of: RVRLASHLRKLRKRLLR (SEQ ID NO:83); RLTRKRGLKLA (SEQ ID NO:76); CRAKRNNFKSA (SEQ ID NO:77); LKWKS (SEQ ID NO:78); KIRVKAGETQKKVIFCSREKVSHL (SEQ ID NO:79); FIPLKPTVKMLERSNHVSRTEVSSNHV (SEQ ID NO:80); DKGMAPALRHLYKELMGPWN (SEQ ID NO:81) and DALKLAIDNALSIT (SEQ ID NO:82).

18. A bone strength and mineralization regulator protein that lacks at least 59% of it sequence from the amino terminal end.

19. A method for discovering a pharmaceutical useful for regulating bone strength or mineralization, comprising the steps:

(a) providing a protein reagent comprising at least one ligand binding site of the BMSR protein;

(b) contacting the reagent from step (a) with a test substance; and

(c) detecting binding between the reagent from step (a) and the test substance, wherein binding indicates that the test substance affects bone strength or mineralization upon administration to a patient.

20. A method as described in claim 19, wherein the protein reagent of step (a) comprises 3 ligand binding sites from a single BMSR protein.

21. A method as described in claim 19, wherein the test substance is a peptide.

22. A composition that improves bone strength and mineralization, the composition comprising a BSMR effector that activates one or more biochemical pathways leading to increased bone mass.

23. The composition of claim 22, wherein the BSMR effector increases alkaline phosphatase activity of bone forming cells by at least 10% compared to cells that are not exposed to the BSMR effector.

24. The composition of claim 22, wherein the BSMR effector is selected from the group consisting of WNT1, WNT2, WNT2B/13, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT10A, WNT10B, WNT11, WNT14, WNT15, WNT16, the 36 kDa cysteine rich frizzled related protein Frzb-1, apolipoprotein, a cysteine rich protein from the CCN family7, Mus musculus FK506 binding protein 8, Mus musculus nuclear protein 95 (Np95) ; GLI-Kruppel family member GLI3, Mus musculus RAN binding protein 9, Mus musculus ISL1 transcription factor, Human signal-transducing guanine nucleotide-binding regulatory (G) protein beta subunit, Mus musculus, casein kinase II, Homo sapiens zinc finger protein 198, Mus musculus, eukaryotic translation elongation factor 2, M.musculus P311, Homo sapiens E2a-Pbx1-associated protein, Homo sapiens NADH dehydrogenase (ubiquinone) Fe-S protein 8, Human Smad anchor for receptor activation (SARA), Homo sapiens AMSH, and ATP6B2.

25. The composition of claim 24, wherein the BSMR effector is a WNT protein.

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25. The composition of claim 22 that further comprises a second morphogenetic protein, wherein the second morphogenetic protein enhances the stimulation of bone mineralization.

27
26. The composition of claim 26, wherein the second morphogenetic protein is selected from the group consisting of bone morphogenetic protein, bone morphogenetic protein 2, bone morphogenetic protein 3, hedgehog protein, endothelial growth factor, and TGF-beta 26.

28
28. The composition of claim 22, wherein the BSMR effector is complexed with a targeting moiety that concentrates the effector at one or more bone producing regions after administration to a patient.

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28. The composition of claim 28, wherein the targeting moiety is selected from the group consisting of a tetracycline, calcein, a bisphosphonate complex, polyaspartic acid, polyglutamic acid, an aminophosphosugar, a peptide known to be associated with the mineral phase of bone, osteonectin, bone sialoprotein, osteopontin, a bone specific antibody, a binding site fragment of a bone specific antibody, and a protein having a bone mineral binding domain.

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29. A method of treating osteoporosis in a human patient, comprising:
(a) providing a composition that comprises a BSMR effector; and
(b) administering a quantity of the composition from step (a) to the patient that is sufficient to increase alkaline phosphatase activity of bone forming cells.

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30. The method of claim 29, wherein the BSMR effector is selected from the group consisting of WNT1, WNT2, WNT2B/13, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT10A, WNT10B, WNT11, WNT14, WNT15, WNT16, the 36 kDa cysteine rich frizzled related protein Frzb-1, apolipoprotein, a cysteine rich protein from the CCN family7, Mus musculus FK506 binding protein 8, Mus musculus nuclear protein 95 (Np95) ; GLI-Kruppel family member GLI3, Mus musculus RAN binding protein 9, Mus musculus ISL1 transcription factor, Human signal-transducing guanine nucleotide-binding regulatory (G) protein beta subunit, Mus musculus, casein kinase II, Homo sapiens zinc finger protein 198, Mus musculus, eukaryotic translation elongation factor 2, M.musculus P311, Homo sapiens E2a-Pbx1-associated protein, Homo sapiens

NADH dehydrogenase (ubiquinone) Fe-S protein 8, Human Smad anchor for receptor activation (SARA), Homo sapiens AMSH, and ATP6B2.

32 ~~31~~. The method of claim 30, wherein the BSMR effector is a WNT protein.

33 ~~32~~. The method of claim 30 ~~29~~, wherein the BSMR effector is complexed with a targeting moiety that concentrates the effector at one or more bone producing regions after administration to a patient.

39 ~~33~~. The method of claim 32, wherein the targeting moiety is selected from the group consisting of a tetracycline, calcein, a bisphosphonate complex, polyaspartic acid, polyglutamic acid, an aminophosphosugar, a peptide known to be associated with the mineral phase of bone, osteonectin, bone sialoprotein, osteopontin, a bone specific antibody, a binding site fragment of a bone specific antibody, and a protein having a bone mineral binding domain.

35 ~~34~~. The method of claim 30 ~~29~~, further comprising an additional step of administering a second morphogenetic protein at least 24 hours prior to step (b).

36 ~~35~~. The method of claim 35 ~~34~~, wherein the second morphogenetic protein is selected from the group consisting of bone morphogenetic protein, bone morphogenetic protein 2, bone morphogenetic protein 3, hedgehog protein, endothelial growth factor, and TGF-beta 26.